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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/322,289	05/28/1999	DALE B. SCHENK	15270-004740	7773

20350 7590 02/24/2005

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EXAMINER	
TURNER, SHARON L	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 02/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/322,289	Applicant(s) SCHENK, DALE B.	
	Examiner Sharon L. Turner	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,6-8,10-12,14,15,17,21-28,31-58 and 60-102* is/are pending in the application.

4a) Of the above claim(s) *25-28,33,34,38-58 and 60-81* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,6-8,10-12,14,15,17,21-24,31,32,35-37 and 82-102* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *See Continuation Sheet* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 August 2004* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims subject to restriction and/or election requirement are 1,2,4,6-8,10-12,14,15,17,21-28,31-58 and 60-102.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11-10-04 has been entered.

2. The amendment filed 8-26-04 and 8-30-04 have been entered into the record and have been fully considered.

3. Claims 1-2, 4, 6-8, 10-12, 14-15, 17, 21-28, 31-58, and 60-102 are pending.

4. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

5. As a result of Applicant's amendment, all rejections not reiterated herein have been withdrawn.

Rejections Maintained

Election/Restriction

6. Applicant's election with traverse of Group I, claims 1-24, 29-32 and 35-37, species A drawn to Abeta in Paper No. 14 is acknowledged. The traversal is on the ground(s) that the species are nonmutually exclusive. This is not found persuasive because while antibody cross-reactivity is well known, the specific antibodies recited for example in claims 25-28 may be generated via different peptide structures which results in alternative immunoreactivity, i.e., the recognition of distinct epitopes. Thus, while

some antibodies may cross react, the antibodies as recited in the nonelected claims are different and are capable of different use, i.e., they are patentably distinct. Accordingly the species are in fact mutually exclusive and capable of separable use: It is also true that a search of antibodies to a single recited epitope would not necessarily reveal antibodies reactive to an alternative epitope, and thus the searches are not co-inclusive even to the generic recitation as recited in the claims, i.e., an antibody which binds Abeta may or may not recognize the recited epitope. For these reasons, the requirement is still deemed proper and is therefore made FINAL.

Applicants argue in the response of 5-17-02 that claims 35-37 are part of Group I. Applicant's further argue that the Abeta epitopes are species within the Abeta genus and are not mutually exclusive.

Applicant's arguments filed 5-17-02 have been fully considered. Claims 35-37 were properly directed to the invention of Group I and were inadvertently omitted by the Examiner. Applicant's arguments in traverse of the species election requirement have been fully considered but are not persuasive. As set forth in MPEP 806.04(f), the general test as to when claims are restricted, respectively, to different species is the fact that one claim recites limitations which under the disclosure are found in a first species but not in a second, while a second claim recites limitations disclosed only for the second species and not the first. This is frequently expressed by saying that claims to be restricted to different species must recite the mutually exclusive characteristics of such species.

In instant case particular species are recited in a first species and not in a second

species while the second species recites limitations disclosed only for the second species and not the first. For example, claim 25 is directed to residues 1-5 while claim 41 is directed to residues 13-28. Moreover, as particular "species" are in fact defined genera or subgenera, restriction for examination purposes is proper in that the search of the multiple genera and subgenera bear undue burden upon the Examiner for search and examination in a single case. Further, it is noted that the genera and subgenera are defined by separate characteristics as claimed and thus may be mutually exclusive and non-coextensive. It is not true that an antibody that binds within residues 1-5 for example, would necessarily bind any other peptide epitope of Abeta such as residues 1-10, 1-16 or otherwise. As set forth previously, rejoinder amongst the generic, sub-generic and/or species claims would only be considered upon the indication of an allowable generic claim that properly linked the claimed inventions sharing the same characteristics. Applicants have designated Abeta as the elected invention. As no claim is indicated allowable, this point is deemed moot with respect to any rejoinder and accordingly the restriction/species election requirement is maintained.

7. Claims 25-28, 33-34 and 38-55 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 14.

8. Newly submitted claims 56-58 and 60-81 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The claims recite patentably distinct methods that differ in reagents, steps, outcomes

and effects. The searches are non-coextensive and a reference against any one element would not necessarily be relevant to any other.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 56-58 and 60-81 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

9. Newly submitted claim 82-102 will be examined as being drawn in part to the previously examined invention.

10. Applicant's remarks in traversal of the restriction are noted and reconsideration upon the indication of allowable subject matter is proper and will be considered at that time.

Claim Objections

11. Claims 14-15 and 91-92 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The base claims (1 and 82) each newly stipulate that the antibody is "a chimeric or humanized antibody, or a human monoclonal antibody and the antibody is of isotype human IgG1." Claims 14 and 91 stipulate that the antibody is polyclonal and thus does not apparently futher limit chimeric, humanized or human monoclonals. Claims 15 and

92 stipulate that the antibody is monoclonal. However, this appears to further broaden from human monoclonals.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1-2, 4, 6-8, 10-12, 14-15, 17, 21-24, 31-32, 35-37 and 82-102 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-36 of U.S. Patent No. 6,761,888. Although the conflicting claims are not identical, they are not patentably distinct from each other because the issued '888 patent contains claims drawn to prophylactic and therapeutic treatment of Alzheimers via administration of humanized or chimeric antibody to an epitope within a beta 1-7 with noted claim limitations corresponding to instant including of the IgG1 class/subclass (claim 19) route of administraion, quantity and patient sample as instantly claimed. The 1-7 epitope is a species which would render obvious instant generic recitation to Abeta peptide specific antibodies. Thus, the '888 claims , particularly claim 19, renders obvious instant claims.

14. Claims 1-2, 4, 6-8, 10-12, 14-15, 17, 21-24, 31-32, 35-37 and 82-102 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 of U.S. Patent No. 6,743,427. Although the conflicting claims are not identical, they are not patentably distinct from each other because the issued '888 patent contains claims drawn to prophylactic and therapeutic treatment of Alzheimers via administration of humanized or chimeric antibody to an epitope within a beta 1-12 with noted claim limitations corresponding to instant including of the IgG1 class/subclass (claim 1) route of administraion, quantity and patient sample as instantly claimed. The 1-12 epitope is a species which would render obvious instant generic recitation to Abeta peptide specific antibodies. Thus, the '427 claims, particularly claim 1, renders obvious instant claims.

Claim Rejections - 35 USC § 102 or 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 1-2, 4, 6-8, 10-12, 14-15, 17, 21-24, 31-32, 35-37 and 82-102 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nettleship et al., EP 613007, Aug. 31, 1994, Walker et al., J. Of Neuropath. & Exp. Neurol., 53(4):377-83, 1994(a), US 5,576,814, Better et al., file d 12. 27, 1994, issued 11-19-1996 and Friedland et al., Mol. Neurobiol., 9(1-3):107-113, 1994.

Nettleship et al., teach antibodies useful in the diagnosis and treatment of mammals suffering from Alzheimer's Disease, see in particular column 7, line 39-column 8, line 18. The antibodies are beta-amyloid peptides, particularly in beta-sheet conformation, but also include antibodies to alternative fragments, see in particular column 1, line 52-column 2, line 56. It is understood that the functional embodiment which characterizes the diagnostic and therapeutic relationship as disclosed in Nettleship hinges on the binding of the antibodies to the beta-amyloid peptides, see in particular reference in paragraph spanning columns 7-8 and reference to numerous assay systems suitable to detect agents which bind, column 8, lines 6-15. While applicants separate claims to prophylaxis, the noted treatment is in and of itself noted to be a prophylaxis of disease in that it is an effective treatment. In addition, the compositions are pharmaceutical compositions which include formulations for parenteral administration (other than by intestinal, i.e., subcutaneous, intravenous, etc., as understood by the skilled artisan), see in particular column 8, lines 19-42. Thus, the reference appears to be enabling for the determination of appropriate doses and routes of administration suitable for such binding to occur. Such would thus render obvious to the skilled artisan the dosage recitations of claims 22-23 and 95-96. Nettleship et al.,

teach the use of alternatively produced Abeta antibodies including to peptides which have adopted a random coil or alpha-helix conformation and to antibodies which are genetically engineered, antibody fragments, chimeric antibodies, recombinantly produced antibodies, and "humanized or murinized" antibodies as generated by replacement of CDR regions, see in particular column 5, lines 42-column 6, line 20. Thus, the reference appears to be enabling for the determination of appropriate doses and routes of administration suitable for such binding to occur. Nettleship et al., teach the use of alternatively produced Abeta antibodies including to peptides which have adopted a random coil or alpha-helix conformation and to antibodies which are genetically engineered, antibody fragments, chimeric antibodies, recombinantly produced antibodies, and "humanized or murinized" antibodies as generated by replacement of CDR regions, see in particular column 5, lines 42-column 6, line 20. Thus the reference teaches the variable antibodies of claims 1, 9-15, 17, 21 and 88-92. It is noted that the polyclonal sera would inherently include multiple antibodies and Ig isotypes. Moreover, the artisan well recognizes chimeric, humanized and human monoclonals of the IgG1 class as further evidenced below. It is further noted that the patient population includes mammals and thus would encompass humans of various risk factors, symptoms and ages as recited in claims 2, 4, 6-8 and 83-87. The reference as a whole evidences multiple assay procedures for binding amyloid and broadly teaches the use of all antibodies of the invention as useful in the diagnosis and treatment of mammals suffering from Alzheimer's, see in particular column 8 and also columns 5-7. The Nettleship reference teaches administration of Abeta antibodies effective in the treatment of Alzheimer's disease. Thus, any amount, route of administration, etc., effective for the treatment of Alzheimer's would be provided or enabled by the reference so long as the antibody specifically binds to Abeta. Claims 10

and 88 are directed to human antibodies. Nettleship teaches making and using human antibodies at for example, column 6, lines 10-21 and lines 31-40. Claim 35-37 and 100-102 are directed to general administration procedures of antibodies including monitoring levels in patients, administration for at least six months and in sustained release compositions. Nettleship et al., teach the administration of antibodies in pharmaceutical preparations and the compositions are effective in the treatment of Alzheimer's disease. Thus, as disclosed in particular at column 8, lines16-42 the Nettleship reference is enabling for antibody administration within the skill in the art including based upon monitoring levels within the blood of a patient, for a period of at least six months and in sustained release compositons.

Nettleship does not teach the selection of the IgG1 class/subclass of antibody, while it does teach chimeric, humanized or human monoclonals with specificity of beta amyloid for treatment.

Walker et al., 1994 (a) teach in vivo labeling of cerebral amyloid with monoclonal antibody 10D5 in nonhuman primates. The anitbody is murine and interacts selectively to beta amyloid in vivo. The antibody is IgG1 kappa light chain and whole antibody or Fab fragments were administered at a dosage of 25 mg/kg im. Walker notes specific binding to amyloid plaques in vivo.

Walker et al., does not specifically teach administration in humans. However, Walker suggests that the methodology would be useful and desirable in patients with Alzheimer's disease, see in particular Discussion pp. 381-382. Walker does not teach administration of the antibody for treatment purposes.

However, Nettleship motivates the artisan to provide antibodies that specifically bind beta amyloid to patients for treatment. Further Nettleship motivates the artisan to alter such immunospecific antibodies to chimeric or humanized monoclonal form to

abrogate hyperimmunogenicity. Specifically, Nettleship teaches that the greatest deterrence to the administration to humans of antibodies produced in non-human sources is the risk of hyperimmunogenicity due to the presence of constant regions from the species in which these antibodies are produced. Genetically engineered antibodies which retain the epitope specificity of monoclonal antibodies are now known in he art and provide a less immunogenic molecule. Such genetically engineered antibodies are contemplated in the present invention, see in particular page 4, column 2, lines 31-53 with specific reference to chimeric and humanized forms in addition to human monoclonals. Thus, one of skill in the art would be motivated to provide the Walker monoclonal with proper epitope specificity of the IgG1 class to humans as taught by Nettleship in modified chimeric or humanized form so as to abrogate hyperimmunogenicity.

Further to support the ability of the artisan to make and use such chimeric or humanized monoclonals, Better et al., US 5,576,184 teaches chimeric or humanized monoclonals of the IgG1 class/subclass that provide for the advantages to decreased hyperimmunogenicity as well as prolonged half-life, thereby motivating the artisan to selection of such procedures for producing the chimeric or humanized 10D5 antibody and to reatain the benefits of reduced clearance of the IgG1 class/subclass. Thus, Better further motivates the artisan to selection of the IgG1 class/subclass and specifes further the methods of the artisan in producing such chimeric or humanized monoclonals of the IgG1 class/subclass where the antibody is engineered to retain the epitope specificity desired. Better further evidences an expectation of success in making the desired chimeric or humanized monoclonal as well as for providing the superior advantages of reduced hyperimmunogenicity and reduced clearance in vivo.

Further as to the specific quantity of administration, Friedland et al., teach in vivo administration to mice of murine monoclonal antibody 10H3 which recognizes beta amyloid at the dosage of 10 ug to a mouse. This quantity correlates to at least 10 mg/kg body weight based on an average mouse weight of 10 g. Fab fragments were labeled with 99mTc for visualization and biodistribution was studied, see in particular Figures 1-2. Thus, Friedland motivates the artisan to select the proper dosage for in vivo administration in mammals such as human.

Thus, for the combined aforementioned reasons, the claimed invention is rendered obvious in light of the cumulative reference teachings and the noted advantages with the use of chimeric or humanized monoclonals of the IgG1 class/subclass for in vivo human administration.

Status of Claims

17. No claims are allowed.

Conclusion

18. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (571) 272-0894. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached at (571) 272-0961.

SHARON L. TURNER, PH.D.
PATENT EXAMINER

Sharon L. Turner, Ph.D.
February 22, 2005